L17 ANSWER 16 OF 36 CANCERLIT
ACCESSION NUMBER: 97620976 CANCERLIT
DOCUMENT NUMBER: 97620976
TITLE: **Immunotherapy** of ovarian cancer with anti-CD3/antitumor bi-mAb: Improvement via CD28 costimulation (Meeting abstract).
AUTHOR: Mazzoni A; Canevari S; Jung G; Mezzanzanica D; Colnaghi M I
CORPORATE SOURCE: Istituto Nazionale Tumori, Milan, Italy 20133.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)** 38 A558.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19980417
Last Updated on STN: 19980417

AB A major limitation to **immunotherapy** of ovarian carcinoma based on the use of anti-CD3/antitumor bispecific monoclonal antibodies (bi-mAb) is the need for preactivation of effector cells ex vivo, since crosslinking of the TCR-CD3 complex per se may lead to T cell nonresponsiveness or even apoptosis. The bi-mAb OC/TR, which recognizes the **folate** binding protein (FBP) overexpressed in 90% of ovarian carcinomas and the CD3 molecule on T cells, has demonstrated efficacy in a clinical setting. Here we investigated the possibility of delivering accessory signals to OC/TR-retargeted peripheral blood mononuclear cells (PBMC) via an anti-FBP/anti-CD28 bi-mAb. Coculture of resting PBMC from healthy donors with OC/TR, anti-FBP/anti-CD28 bi-mAb and FBP+ tumor cell lines resulted in a highly activated phenotype of effector cells and in a significant growth inhibition of the target cells without an increase in OC/TR-redirected lysis. The in vitro inhibition of tumor cell growth was mediated mainly by soluble factors, which were active on both FBP+ and FBP- (bystander effect) cell lines. The effector cells also released **IL2**, thus supporting their growth in an autocrine loop. In vivo experiments in athymic mice demonstrated that crosslinking between tumor and effector cells for 36 hours via the combination of the two bi-mAb was sufficient to achieve T cell activation and a significant delay in tumor progression.